CLAIMS

WE CLAIM:

1. A chimeric protein kinase having an inhibitor binding site comprising amino acid residues of a first protein kinase which bind an inhibitor and amino acid residues of a second protein kinase which do not bind the inhibitor.

2. The chimeric protein kinase of claim 1 wherein the first protein kinase is not crystallizable and the second protein kinase is crystallizable.

3. A crystal comprising a chimeric protein kinase having an inhibitor binding site comprising amino acid residues of a first protein kinase which bind an inhibitor and amino acid residues of a second protein kinase which do not bind the inhibitor.

4. The crystal of claim 3 wherein said crystal diffracts to greater than 5 Å.

5. A chimeric protein kinase comprising inhibitor binding site amino acid residues from a first protein kinase selected from the group consisting of IKK-β, Map/ERK, JNK, GSK-3, Akt, NIK and MEK and non-inhibitor binding site amino acid residues of a second protein kinase selected from the group consisting of p38 and ERK2, Src, CAPK, CK1, EGF-S, CDK2 and FGF-R.

6. The chimeric protein kinase of claim 5 wherein the inhibitor binding site is an ATP binding site.

7. The chimeric protein kinase of claim 5 wherein the inhibitor binding site is a non-ATP binding site.

8. The chimeric protein kinase of claim 7 wherein the second protein kinase is p38 which comprises inhibitor binding site residues of the protein first protein kinase.

9. The chimeric protein kinase of claim 8 wherein the first protein kinase is IKK-β.

10. The chimeric protein kinase of claim 9 wherein p38 comprises amino acid changes of His 107 to Tyr, Glu81 to Pro and Leu353 to Ala.

11. The chimeric protein kinase of claim 8 wherein the first protein kinase is Map/ERK.

12. The chimeric protein kinase of claim 11 wherein p38 comprises amino acid changes of Lys79 to Asn, Glu81 to Pro and the C-terminal sequence PPLDQE to THAASI.

13. The chimeric protein kinase of claim 8 wherein the first protein kinase is JNK.

14. The chimeric protein kinase of claim 13 wherein p38 comprises amino acid changes of Thr106 to Met, Tyr35 to Gln, His107 to Glu, and Leu75 to Met.

15. The chimeric protein kinase of claim 8 wherein the first protein kinase is MEK

16. The chimeric protein kinase of claim 15 wherein p38 comprises amino acid changes of Lys79 to Asn, Glu81 to Pro and the C-terminal sequence PPLDQE of p38 is changes to THAASI.

17. The chimeric protein kinase of claim 8 wherein the first protein kinase is GSK-3.

18. The chimeric protein kinase of claim 15 wherein p38 comprises amino acid changes of Lys79 to Asp, Glu81 to Cys, His107 to Asp and the C-terminal sequence PPLDQE to PHARIQ.

19. The chimeric protein kinase of claim 8 wherein the first protein kinase is Akt.

20. The chimeric protein kinase of claim 19 wherein p38 comprises the amino acid changes of Lys79 to Arg, Glu81 to Pro, His107 to Tyr and the C-terminal sequence PPLDQE to FPQFSV.

21. The chimeric protein kinase of claim 8 wherein the first protein kinase is NIK.

22. The chimeric protein kinase of claim 21 wherein p38 comprises amino acid changes of Lys79 to Arg, Glu81 to Val, His107 to Asn and the C-terminal sequence PPLDQE to TLAVKE.

23. A crystal comprising a chimeric protein kinase which comprises inhibitor binding site residues of a first protein kinase selected from the group consisting of IKK-β, Map/ERK, MEK, JNK, GSK-3, AKT and NIK and non-inhibitor binding site residues of a second protein kinase selected from the group consisting of p38, ERK2, Src, CAPK, CK1, EGF-R, CDK2 and FGF-R.

24. The crystal of claim 23 wherein said crystal diffracts to greater than 5 Å.

25. A method for identifying inhibitor molecules capable of affecting the activity of a first protein kinase comprising:

a) preparing a chimeric protein kinase comprising inhibitor binding site residues of the first protein kinase and non-inhibitor binding site residues of a second protein kinase wherein said chimeric protein kinase is cystallizable;

b) growing a crystal of said chimeric protein kinase;

c) solving the structure of said crystal using X-ray crystallography methods; and

d) using said structure to design inhibitor molecules capable of affecting the activity of the first protein kinase.

26. The method of claim 25 wherein the first protein kinase is selected from the group consisting of IKK-β, Map/ERK, JNK, MEK, GSK-3, Akt and NIK.

27. The method of claim 25 wherein the second protein kinase is selected from the group consisting of p38, ERK2, Src, CAPK, CK1, EGF-R, CDK2 and FGF-R.

28. The method of claim 25 wherein the inhibitor binding site is an ATP binding site.

29. The method of claim 25 wherein the inhibitor binding site is a non-ATP binding site.

30. The method of claim 29 wherein the inhibitor binding site is selected from the group consisting of PD98059 binding site and suldinac sulfide binding site.

31. The method of claim 25 wherein the first protein kinase is IKK-β and the second protein kinase is p38.

32. A protein kinase inhibitor binding site whose amino acid sequence corresponds to an amino acid sequence of, and has three-dimensional structural homology to, a protein kinase domain starting with linker L5 (residues 76-83) that joins helix C (residues 63-75) with β4 (residues 84-89), the crossover connection (L7) (residues 106-109) and ending at a C-terminus (βL16) (residues 310-336), wherein said domain is described to according to residues of p38.

33. The protein kinase inhibitor binding site of claim 32 wherein the protein kinase domain is derived from a protein kinase selected from the group consisting of p38, IKK-β, Map/ERK, JNK, MEK, GSK-3, Akt and NIK.